

REMARKS

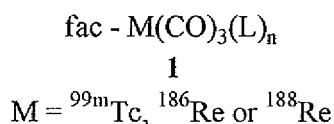
Applicants elect Group II, claims 12-22, with traverse. Applicants specifically request rejoinder of the process claims upon an indication of allowability of the product claims.

Applicants traversal is based on the fact that a special technical feature does exist in the claims such that unity of invention is proper. One of ordinary skill in the art would appreciate that the chemistry of a carbonylated metal is different, requiring the use of oxygenated ligands (L) in order to stabilize the metal chelate (as defined in the claims of patent WO96/20054), than that of the claimed invention. To illustrate, the Examiner has restricted the claims into the following six groups:

1. Group I, claim(s), 1-11, drawn to compound of formula I
2. Group II, claim(s) 12-22, drawn to a radiolabeled liposome
3. Group III, claim(s) 23-29 and 40, drawn to a method of making a radiolabeled liposome comprising mixing a liposome having an outer space and an inner volume, wherein the pH of the inner volume of the liposome is less than the pH of the outer space of the liposome, with a compound of formula I.
4. Group IV, claim(s) 30-34 and 41, drawn to a method of making a radiolabeled liposome comprising mixing a liposome having an outer space and an inner volume, wherein a drug comprising at least one thiol group is incorporated within the inner volume of the liposome, with a compound of formula I.
5. Group V, claim(s) 25 and 26, drawn to the use of radiolabeled liposomes as an imaging agent
6. Group VI, claim(s) 37-39, drawn to the use of radiolabeled liposomes to treat a disease.

Applicants contend that a special technical feature has been shown in the claims because WO96/20054 does not disclose Applicants' claimed invention of Claims 1-41. Publication WO 96/20054 defines a carbonylated metal (1) with oxygenated ligands (L). The chemistry of a carbonylated metal is different than that of the claimed invention and requires the use of oxygenated ligands (L) in order to stabilize the metal chelate (as defined in the claims of patent

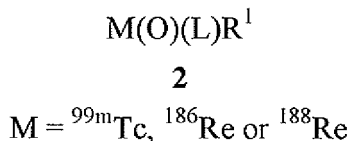
WO96/20054). In short, the atomic properties of the metal are dramatically different relative to claims in question. The carbonyl ligands encompass substantially



L = is i) monodentate ligands ii) bidentated ligand and monodentate ligand iii) tridentated ligand
n = is a charge of the ligand increased with 1 + charge

different chemistries that change the electronics of the metal atom, requiring unique poly-oxygenated ligands to stabilize the complex. Publication WO 96/20054 defines the use poly-oxygenated ligands and does not refer to the use of alternative poly-hetero ligands. The ligands claimed in this are uniquely to the carbonylated metal. There is no mention of alternative ligand substitutes for the chemistries outlined in WO 96/20054. The chemistry is sufficiently different that the instant application does define a special technical feature over the prior art. Accordingly, Applicants respectfully request the claims be treated with unity of invention.

As further illustration, the Groups II, II, and IV of the Examiner's restriction define non-obvious changes to an oxo metal core and not a carbonylated metal core. The ligands claimed by Applicants are unique to an oxo metal structure composed of, for example, rhenium and technetium. In addition, the ligands stabilize the oxo metal core via exchange. Typically the M(V) oxo



L = tridentateligand with SNS like configuration

R¹ = thio substituted moities, outlined in patent claims

metal is generated by reduction of the M(VII) metal with an appropriate reducing agent in the presence of a glucoheptanate ligand. This ligand is unstable and temporary. It is used for the *in situ* tin reduction to generate oxo rhenium cores. The glucoheptanate ligand is immediately

exchanged with SXS chelating moieties in order to stabilize the oxo metal core. The SXS ligands are claimed by Applicants, e.g. SNS of Group I.

The claimed structure offers further special technical features that lead to the liposome encapsulated radionuclide in Group II. In addition, the ligands claimed in group I are used to gradient load a liposome with a chelated radionuclide of, for example, formula 1, thereby linking Groups III and IV. Accordingly, special technical features have been disclosed.

Special technical features at least comprise key structures enabling the formation of liposomal encapsulated radionuclides. The core structure of Group I ties together the technical features of Group II (liposome encapsulated radionuclides), Group III and IV (gradient loading procedures for the generation of liposome encapsulated radionuclides).

Group V and VI define various general uses of the complexes disclosed.

Applicants request reconsideration of the restriction. Unity of invention does exist because there is a special technical feature. Applicants request an interview with the Examiner to further discuss this issue.

CONCLUSION

Applicants have elected Group II with traverse and respectfully request consideration of the present application and request that the Examiner call Applicants' attorney at the below listed number if the Examiner believes that such a discussion would be helpful. Applicants specifically petition for a four month extension of time, the fee for which should be charged to deposit account 02-2334.

Respectfully submitted,

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